Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-29. (Canceled)

30. (Currently Amended) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-N-acetylglucosaminyltransferase III activity ~~or β(1,4)-galactosyltransferase activity~~ and comprises the Golgi localization domain of a Golgi resident polypeptide other than ~~the Golgi resident polypeptide that provides the glycosyltransferase activity of said fusion polypeptide~~ β(1,4)-N-acetylglucosaminyltransferase III, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

31. (Currently Amended) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an expression vector which comprises an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-N-acetylglucosaminyltransferase III activity ~~or β(1,4)-galactosyltransferase activity~~ and comprises the Golgi localization domain of a Golgi resident polypeptide other than ~~the Golgi resident polypeptide that provides the glycosyltransferase activity of said fusion polypeptide~~ β(1,4)-N-acetylglucosaminyltransferase III, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

32. (Original) A method according to claim 30 or 31, wherein said polypeptide is IgG or a fragment thereof.

33. (Original) A method according to claim 32, wherein said polypeptide is IgG1 or a fragment thereof.

34. (Original) A method according to claim 32, wherein said polypeptide is a fusion protein that includes a region equivalent to the Fc region of a human IgG.

35-64. (Canceled)

65. (Currently Amended) A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity ~~or β(1,4)-galactosyltransferase activity~~ under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having β(1,4)-N-acetylglucosaminyltransferase III activity ~~or β(1,4)-galactosyltransferase activity~~ comprises the Golgi localization domain of a Golgi resident polypeptide other than ~~the Golgi resident polypeptide that provides the glycosyltransferase activity of said fusion polypeptide~~ β(1,4)-N-acetylglucosaminyltransferase III; and

b. isolating said polypeptide.

66. (Original) A method according to claim 65 wherein said fusion polypeptide comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III or β(1,4)-galactosyltransferase.

67. (Original) A method according to claim 65, wherein said fusion polypeptide further comprises the Golgi localization domain of a heterologous Golgi resident polypeptide.

68. (Original) A method according to claim 67, wherein said Golgi localization domain is the localization domain of mannosidase II.

69-73. (Canceled)

74. (Currently Amended) A method according to claim [[73]] 65, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

75-81. (Canceled)

82. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

83. (Original) A method according to claim 82, wherein said Fc receptor is Fc activating receptor.

84. (Original) A method according to claim 82, wherein said Fc receptor is FcγRIIIA receptor.

85. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

86. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region of said polypeptide.

87. (Original) A method according to claim 86, wherein said nonfucosylated oligosaccharides are hybrid.

88. (Original) A method according to claim 86, wherein said nonfucosylated oligosaccharides are complex.

89. (Original) A method according to claim 65, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

90. (Original) A method according to claim 89, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

91. (Original) A method according to claim 89, wherein said bisected, nonfucosylated oligosaccharides are complex.

92. (Original) A method according to claim 89, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

93. (Original) A method according to claim 89, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

94. (Original) A method according to claim 89, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

95. (Original) A method according to claim 89, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

96-185. (Canceled)

186. (Currently Amended) A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having GnT III activity and at least one nucleic acid encoding a polypeptide having Man II activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having GnT III activity comprises the Golgi localization domain of a Golgi resident polypeptide other than ~~the Golgi resident polypeptide that provides the glycosyltransferase activity of said fusion polypeptide~~ GnT III; and

b. isolating said polypeptide.

187. (Canceled)

188. (Previously Amended) A method according to claim 186 wherein said fusion polypeptide comprises the catalytic domain of GnT III.

189. (Original) A method according to claim 188, wherein said fusion polypeptide further comprises the Golgi localization domain of a heterologous Golgi resident polypeptide.

190. (Original) A method according to claim 189, wherein said Golgi localization domain is the localization domain of mannosidase II.

191-205. (Canceled)

206. (Previously Amended) A method according to claim 186, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

207. (Original) A method according to claim 206, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

208. (Original) A method according to claim 206, wherein said bisected, nonfucosylated oligosaccharides are complex.

209. (Original) A method according to claim 206, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

210. (Original) A method according to claim 206, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

211. (Original) A method according to claim 206, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

212. (Original) A method according to claim 206, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

213-286. (Canceled)

287. (New) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase II, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

288. (New) A method for modifying the glycosylation profile of a polypeptide produced by a mammalian host cell, comprising introducing into said host cell an expression vector which comprises an isolated nucleic acid comprising a sequence encoding a fusion polypeptide, wherein said fusion polypeptide has β(1,4)-galactosyltransferase activity and comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase II, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, and wherein said modified polypeptide has increased Fc-receptor binding or effector function as a result of said modification.

289. (New) A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion polypeptide having β(1,4)-galactosyltransferase activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion polypeptide is expressed in an amount sufficient to modify the oligosaccharides in the Fc region and increase the Fc-receptor binding or effector function of said polypeptide produced by said host cell and wherein said fusion polypeptide having β(1,4)-galactosyltransferase activity comprises the Golgi localization domain of a Golgi resident polypeptide selected from the group consisting of: mannosidase I, mannosidase

II, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase; and

b. isolating said polypeptide.

290. (New) A method according to claim 287 or 288, wherein said polypeptide is IgG or a fragment thereof.

291. (New) A method according to claim 290, wherein said polypeptide is IgG1 or a fragment thereof.

292. (New) A method according to claim 290, wherein said polypeptide is a fusion protein that includes a region equivalent to the Fc region of a human IgG.

293. (New) A method according to claim 289 wherein said fusion polypeptide comprises the catalytic domain of β(1,4)-galactosyltransferase.

294. (New) A method according to claim 289, wherein said fusion polypeptide further comprises the Golgi localization domain of a heterologous Golgi resident polypeptide.

295. (New) A method according to claim 294, wherein said Golgi localization domain is the localization domain of mannosidase II.

296. (New) A method according to claim 289, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

297. (New) A method according to claim 289, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

298. (New) A method according to claim 297, wherein said Fc receptor is Fc activating receptor.

299. (New) A method according to claim 297, wherein said Fc receptor is FcγRIIIA receptor.

300. (New) A method according to claim 289, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

301. (New) A method according to claim 289, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

302. (New) A method according to claim 301, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

303. (New) A method according to claim 301, wherein said bisected, nonfucosylated oligosaccharides are complex.

304. (New) A method according to claim 301, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

305. (New) A method according to claim 301, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

306. (New) A method according to claim 301, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

307. (New) A method according to claim 301, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.